REMARKS

Claims 1, 3-8, and 21-30 are pending in the application.

In the present response, claims 1, 8, and 21-30 have been amended. As provided below, support for the amendments to claims 1, 8, and 21-30 is found throughout the specification as filed. It is believed that no new matter has been introduced.

Applicants gratefully acknowledge the Examiner's withdrawal of the rejection of pending claims 1 and 3-8 under 35 USC § 112, second paragraph made in the previous Office Action.

Reconsideration and allowance of all of the pending claims, as amended, is respectfully requested.

Specification

Paragraph [0607] of the specification as filed is being amended to correct a typographical error.

Priority

According to the Office Action, the disclosure of the prior-filed provisional application No. 60/427,982 allegedly fails to provide adequate enabling support for one or more claims of this application. Specifically, the Office Action alleges that the "...provisional application does not provide support for table 6, which does not obtain the benefit of the priority date...[and]...the effective filing date for said subject matter is 4/3/03." (See page 3 of the Office Action).

Table 6 of the present application lists 184 renal cell carcinoma (RCC) disease genes ranked by the number of samples in which the gene was observed. As amended, independent claim 1 recites a method of diagnosing RCC in a peripheral blood sample of a human by comparing the expression profile of two or more RCC genes to at least one reference expression profile obtained from peripheral blood samples from patients having RCC or peripheral blood samples from disease-free humans and, wherein differential expression of said two or more RCC genes in said comparison is indicative of the presence or absence of RCC in the human. The RCC genes are those listed in **Table 8** of the present application.

Support for independent claim 1, as amended, and its dependent claims 3 through 8, and 21 through 30 is found throughout the disclosure of the prior-filed application. For example, Table 6 of the prior filed application corresponds to Table 8 of the present application.

As stated above, enabling support for amended claim 1 and its dependent claims 3 through 8, and 21 through 30 is also found throughout the disclosure of the present application.

In view of the above, Applicants respectfully submit that both, the parent application (application No. 60/427,982) and the later filed application (application No. 10/717,597) provide enabling support for the amended claims. Priority of the claimed invention to 11/21/2002, as claimed, is respectfully requested.

35 U.S.C. § 112, 1st paragraph, written description, rejections

Claims 1, 3-8, and 21-30 were rejected under 35 U.S.C. § 112, 1st paragraph, as allegedly failing to comply with the written description requirement.

The Office Action alleges that: (1) the specification does not specifically disclose individual genes or combination of genes that can be used to diagnose RCC; (2) individual genes recited in the claims may be differentially expressed in other diseases; (3) it is not known if all genes listed in claim 1 are differentially expressed in an RCC patient as compared to individuals with other diseases (See page 7 of the Office Action); (4) the specification does not show that the correlation observed between gene expression profiles of RCC tumor and disease free tissues are predictive of diagnosis of RCC (See page 8 of the Office Action); the specification does not provide all possible combinations of genes that can be used to differentiate RCC from other tumor diseases (See page 9 of the Office Action); and (5) some of the claimed genes were found present in less than 6 patients which would make the sample size not statistically significant to show possession of the claimed method (See page 10 of the Office Action). The Office Action further asserts that the claims should refer to the sequence identifier found in the specification for each of the polynucleotide sequences.

As noted above, Applicants have amended claim 1 to recite a method of diagnosing RCC in a sample by comparing the expression profile of two or more RCC genes to at least one reference expression profile. The specific RCC genes to be used and their SEQ ID NOs in the specification are recited in the claim.

Applicants respectfully submit that the specification specifically discloses combinations of genes that can be used to diagnose RCC in a patient, as claimed. Specifically, at Example 6, paragraphs [0601] through [0609] of the specification as filed, the genes listed in claim 1 were used to predict if a sample was from an RCC patient or from a disease-free subject. As indicated in Table 8, at page 199, different combinations of genes, using 2, 4, 6, 8, 10, 12, 14, 16, 18, or 20 of the claimed genes, were between 85% and 100% accurate in predicting if a sample was from an RCC patient or from a disease-free subject. The blood samples were from patients at different stages of RCC and from disease-free subjects and were collected during clinical trials as indicated in Example 1, at page 156 of the specification as filed. Applicants submit that the different combinations of genes used in Example 6 to determine the presence or absence of RCC and the results tabulated in Table 8 demonstrate that different combinations of the claimed genes may be used to diagnose RCC in a subject.

Example 6, at pages 197-200 of the specification, uses 2, 4, 6, 8, 10, 12, 14, 15, 18, or 20 of the genes listed in claim 1 to predict if a sample is from an RCC patient or a disease-free subject. This example also shows the accuracy of the different claimed combinations in making such a prediction.

Applicants respectfully submit that the amendments to the claims overcome the written description rejection of claims 1, 3-8, and 21-30 under 35 U.S.C. § 112, 1st paragraph for at least the following reasons: (1) the claims compare the expression profile of two or more RCC genes, thus, the differential expression of individual genes in other diseases is irrelevant; (2) all genes listed in claim 1 are differentially expressed in an RCC patient as compared to disease-free subjects (Table 8); and (3) the specification shows that the correlation observed between gene expression profiles of the claimed genes in RCC tumor and disease free tissues are predictive of diagnosis of RCC; finally, (4) the SEQ ID NO for the specific RCC genes have been identified in the claim.

In view of the above amendments and comments, withdrawal of the written description rejection under 35 U.S.C. § 112, 1st paragraph, is respectfully requested.

35 U.S.C. § 112, 1st paragraph, enablement, rejections

Claims 1, 3-8, and 21-30 were rejected under 35 U.S.C. § 112, first paragraph, allegedly because they lack enablement.

The Office Action alleges that the specification (1) "...does not specifically disclose which individual genes or combination thereof would provide gene expression profiles that can be used to diagnose RCC..."; (2) teaches only one example (Example 6) where gene expression profiles from RCC patients are compared to gene expression profiles from disease-free subjects; and (3) "...only provides examples correlating (but not diagnosing) gene expression profiles..." (See pages 12 through 15 of the Office Action.) The Office Action concludes that undue experimentation would be required to practice the invention.

Applicants respectfully traverse this rejection. As noted above, the specification specifically discloses (in Example 6) combinations of genes that can be used to determine the presence or absence of RCC in a patient. The specification also discloses (in Table 8) the accuracy of these combinations for predicting if a sample is from an RCC patient or from a disease free subject. As indicated in Table 8, at page 199, different combinations of the claimed genes, using 2, 4, 6, 8, 10, 12, 14, 16, 18, or 20 of said genes were between 85% and 100% accurate in predicting if a sample was from an RCC patient or from a disease-free human.

And, as stated above, claim 1 as amended recites a method of diagnosing RCC in a sample by comparing the expression profile of two or more RCC genes to at least one reference expression profile. The specific RCC genes to be examined and their SEQ ID NO in the specification are recited in the claim.

In view of the amendments to the claims and the comments above, Applicants submit that no undue experimentation is required to practice the invention as claimed.

Applicants respectfully submit that the amendments to the claims overcome the above rejection of claims 1, 3-8, and 21-30 under 35 U.S.C. § 112, 1st paragraph for lack of enablement. Withdrawal of the 35 U.S.C. § 112, 1st paragraph, enablement rejection is respectfully requested.

35 U.S.C. § 112, 1st paragraph, new matter, rejections

Claims 1, 3-8, and 21-30 were rejected under 35 U.S.C. § 112, 1st paragraph, as containing new matter.

According to the Office Action, "...the instant specification does not provide support for the method of using any one or any combination of the recited genes in the amended claims...[and]...applicant must disclose where in the specification support for the entire scope of the amendment(s) and/or new claims can be found." (See page 18 of the Office Action.)

As amended, claim 1 recites a method of determining the presence or absence of RCC in a sample by comparing the expression profile of two or more RCC genes to at least one reference expression profile. The specific RCC genes to be used and their respective SEQ ID NO in the specification are recited in the claim. Support for the entire scope of amended claim 1 is found in the specification as filed. For example, paragraph [0536] describes predicting RCC vs RCC-free using the RCC genes listed in claim 1, the genes listed in claim 1 also correspond to those used in Example 6 of the instant specification, Table 8 tabulates the accuracy of predicting the presence or absence of RCC in a human using 2, 4, 6, 8, 10, 12, 14, 16, 18, or 20 of the genes listed in claim 1, and Table 4 indicates the SEQ ID NO of the genes used. Thus, claims 1, 3-8, and 21-30 do not represent new matter.

Withdrawal of the 35 U.S.C. § 112, 1st paragraph, new matter, rejection is respectfully requested.

35 U.S.C. § 103(a) rejections

Claims 8-20 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over McKiernan (US Patent 6,087,098), in view of Young (Am. J. Path. 2001; 158:1639-1651), Golub (Science, 1999; 286:531-527), and Liu (Inf. Immun. 2001; 69:2788-2796).

According to the Office Action, McKiernan allegedly teaches methods of diagnosing prostate cancer using peripheral blood samples by comparing gene expression levels but does not specifically teach the genes recited in the claims. Young is cited for teaching the use of gene expression profiling for diagnosis or classification of renal cell carcinomas and for teaching that Galectin 3 is differentially expressed in RCC and can be used for diagnosis. Golub is cited as teaching cancer

classification based on gene expression by using statistical analysis. Liu is cited as teaching that TLR2 is predominantly distributed in monocytes/macrophages and involved in the signal pathway of the immune system. The Office Action therefore alleges that it would have been prima facie obvious to one of ordinary skill in the art to generate a method comprising comparing the gene expression profile of one or more genes (specifically TLR2) from peripheral blood samples using known statistical tools to analyze the expression pattern.

Applicants respectfully traverse this rejection. As noted above, claim 1 has been amended to recite a method of diagnosing RCC in a sample by comparing the expression profile of **two or more RCC genes** to at least one reference expression profile. The specific RCC genes to be used and their SEQ ID NO in the specification are recited in the claims. According to MPEP § 706.02(j), for a 103 rejection to be proper, the prior art reference (or references when combined) must teach or suggest all of the claim limitations. Applicants respectfully submit that McKiernan, Ralph, Young, Golub, or Liu, neither alone nor in combination, teach or suggest the entire scope of the claims. None of these references teach or suggest a method comparing the expression profile of two or more RCC genes. The references do not teach genes having the specific sequences listed in the claim and used to diagnose RCC. Thus, Applicants submit that all the elements of the amended claims are not taught by the cited references either alone or when combined.

Based on the foregoing, withdrawal of the 35 U.S.C. § 103(a) rejection is respectfully requested.

CONCLUSION

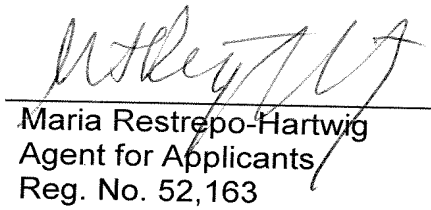
In view of the above amendments and remarks Applicants respectfully submit that the rejections of record have been overcome, and the application is now in form of allowance. Accordingly, allowance of the application on the merits is respectfully requested.

A request for continued examination (RCE) and a petition for a three-month extension of time to file this response accompany this paper.

During the pendency of this application please treat any reply requiring a petition for extension of time for its timely submission as containing a request therefore for the appropriate length of time. The Commissioner is hereby authorized to charge all

required extension of time fees during the entire pendency of this application to Deposit Account No. 01-1425.

If any outstanding issue remains, the Examiner is invited to contact the undersigned agent for a discussion of a mutually agreeable solution.



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